REMARKS

Formal Matters

Claims 26, 27, 29, 30 and 32 are pending after entry of the amendments set forth herein.

Claims 26, 27, 29, 30 and 32 were examined and rejected.

Claims 27 and 30 are amended for clarity. Support for the amendments is found at, for example, page 7, line 7; page 33, lines 5-6; and page 37, line 4. Accordingly, no new matter is added.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Request for Interview

The Applicant respectfully requests a telephonic interview with Examiner Ungar *prior to* the mailing of the next Office Action, if any rejections remain after consideration of the arguments set forth below. The Applicant's representative James Keddie can be reached at (650) 833 7723.

The Response in General

Claim amendments

The claims have been amended for clarity.

The phrase "increased transcription from a p53 binding site controlled promoter" has been rephrased to "increased activity of a promoter having a p53 binding site".

This amendment is supported on page 7, line 7, of the specification, where the phrase "ING2 activates p53 binding site controlled promoters" is set forth.

In view of the MPEP's guidance that support for a claim amendment need not be *in haec verba*, the Applicants submit that this amendment is fully supported.

Prior interview

In a telephonic interview with Exrs. Ungar and Eyler on May 3, 2004, prior to the outstanding Office Action, Exr. Eyler indicated that the basis of all remaining rejections is the assertion that no data is shown for SEQ ID NO:8 in the instant application.

Examiner Eyler stated that post-filing data demonstrating the utility of SEQ ID NO:8, or suitable reasoned argument supporting the same, would be sufficient to withdraw the rejections.

Prior response

SEQ ID NO:8 is asserted to modulate activity of a promoter having p53 binding sites. p53, a well known transcription factor involved in tumor suppression, binds to p53 sites in promoters to control transcription.

In response to the prior Office Action, and in view of Exr. Eyler's comments during the interview, the Applicants pointed to a significant amount of data in support of this assertion. This data relates to four polypeptides (SEQ ID NOS:2, 4 and 6) which are splice variants encoded by the same gene as SEQ ID NO:8, and which share an identical 200 amino acid domain with SEQ ID NO:8. As discussed in the prior response, *all* of these polypeptides increase activity of a promoter having p53 binding sites (see Fig. 12 of the specification).

The publication by Shiseki et al (provided as Exhibit C of the prior response) supports the Applicants' analysis above. Shiseki et al. shows that p28ING5, which an amino acid sequence that differs from SEQ ID NO:8 by only 13 amino acids at the N-terminus and also has the 200 amino acid domains of SEQ ID NOS:2, 4 and 6, has activity in modulating transcription from a promoter having a p53 binding site.

In conclusion, based on the data in the application with the polypeptides of SEQ ID NOS:2, 4, and 5 which share a common sequence with SEQ ID NO:8, one of skill in the art would reasonably conclude that SEQ ID NO:8 necessarily has the same activity as SEQ ID NOS: 2, 4, 6. Indeed, as shown by Shiseki et al, this conclusion would be correct.

A brief summary of the Applicant's prior arguments, including figures showing alignments of SEQ ID NO:8 with SEQ ID NOS: 2, 4, 6 and p28ING5, is attached hereto as Exhibit A.

This Office Action

The instant Office Action states that the Applicant's arguments were generally found unpersuasive for the following reasons:

Reason A: Shiseki's paper (i.e., Exhibit C submitted with the prior response) does *not* show that p28ING5 (a protein that is identical to SEQ ID NO:8, except for the N-terminal 13 amino acids) increases activity of promoter having p53 binding sites; and

Reason B: the mechanisms by which ING family proteins (of which SEQ ID NO:8 is a member) modulate p53 vary greatly and have not been fully elucidated, therefore the utility of those proteins is unknown.

Response

With respect to Reason A and in direct contrast to the Office's statements, the Applicants note that Shiseki's paper *does* show that p28ING5 increases activity of promoter having p53 binding sites. As shown in Fig. 2B and as explicitly discussed in p. 3475 col. 2, lines 17-18 and p. 2377 col. 1, lines 6-15 of Shiseki's paper, p28ING5 increases the activity of the *p21/waf-1* promoter, which is well known to contain p53 binding sites.

For the convenience of the Examiner, a relevant section of Shiseki's disclosure (p. 2377, col. 1, lines 9-15) is copied below, and statements explicitly supporting the Applicants position are underlined.

> p28ING5 on a p53-responsive promoter. *p21/waf-1* is a well-characterized p53-regulated gene of which the promoter contains consensus sequences of the p53-binding sites (26). Our results show that p29ING4 or p28ING5 overexpression activates the *p21/waf-1* promoter, and increases p21/WAF1 protein in RKO cells, but not in RKO-E6 cells. Thus, p29ING4 and p28ING5 can modulate p53 transcriptional activity. The modest activation of the *p21/waf1* pro-

In view of the above, the Applicants respectfully submit that Shiseki demonstrates that p28ING5, a protein that is identical to SEQ ID NO:8 except for 13 amino acids at its N-terminus, *does* increase the activity of a promoter having p53 binding sites.

Further, with respect to Reason B, the Applicants note that it is well established that an understanding of the scientific theory or principle underlying an invention is not a requirement for

patentability.[1] Thus, assertions regarding the molecular mechanism by which SEQ ID NO:8 (or any of the other ING family proteins) modulates p53 activity simply have no bearing on the patentability of SEQ ID NO:8.

In view of the above and the arguments set forth in the prior response (summarized in Appendix A of this response), the Applicants submit that one of skill in the art would reasonably conclude that SEQ ID NO:8, like the splice variants of SEQ ID NO:8 discussed above, increase the activity of promoters having p53 binding sites. As such, SEQ ID NO:8 may be used to modulate apoptosis of a cell.

As a final note, MPEP § 2164.07 states that" "the applicant does not have to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt."[2] Instead, evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true"

The Applicants respectfully submit that the remaining rejections may be withdrawn.

Rejection of claims under 35 U.S.C. § 101 (section 5 of Office Action)

All claims are rejected under 35 U.S.C. § 101 for lacking patentable utility.

The Applicants respectfully submit that this rejection has been adequately addressed in the general discussion above, and, accordingly, this rejection may be withdrawn.

Rejection of claims under 35 U.S.C. § 112, first paragraph (section 6 of Office Action)

Claim 27 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Applicants respectfully traverse this rejection.

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[1] See, e.g., In re Gazave, 379 F.2d 973, 978, 154 USPQ 92, 96 (CCPA 1967); In re Chilowsky, 229 F.2d 457, 462, 108 USPQ 321, 325 (CCPA 1956) and Philip Morris, Inc. v. Brown & Williamson Tobacco Corp., 641 F. Supp. 1438, 1483 n.13, 231 USPQ 321, 355 n.13 (M.D. Ga. 1986).

[2] Citing In re Irons, 340 F.2d 974, 978, 144 USPQ 351, 354 (CCPA 1965).

Without wishing to acquiesce to the correctness of this rejection, the claims have been amended to recite polypeptides that *increase activity of a promoter having a p53 binding site when introduced into a mammalian cell.* The Applicants respectfully submit that in view the amendment and the above general discussion, this rejection has been adequately addressed and may be withdrawn.

Rejection of claims under 35 U.S.C. § 112, first paragraph (section 7 of Office Action)

All claims are rejected under 35 U.S.C. § 112, first paragraph, because one of skill in the art would not know how to use an invention with no apparent utility.

The Applicants respectfully submit that this rejection has been adequately addressed by the general discussion above, and, accordingly, this rejection may be withdrawn.

Rejection of claims under 35 U.S.C. § 112, first paragraph (section 8 of Office Action)

Claim 27 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Without wishing to acquiesce to the correctness of this rejection, the claims have been amended to recite polypeptides *increase activity of a promoter having a p53 binding site when introduced into a mammalian cell.* The Applicants respectfully submit that in view the amendment and the above general discussion, this rejection has been adequately addressed and may be withdrawn.

Rejection of claims under 35 U.S.C. § 112, first paragraph (section 9 of Office Action)

Claim 27 is rejected for reciting matter that is assertedly unsupported by the instant specification.

The Applicants note that this rejection was originally issued because the claims recited the phrase "binds to an inhibitor of apoptosis protein (IAP)".

Since this phrase no longer present in the claims, this rejection is moot.

Rejection of claims under 35 U.S.C. § 112, first paragraph (section 10 of Office Action)

Claims 27, 30 and 32 are rejected for reciting matter that is assertedly unsupported by the instant specification. The Applicants respectfully traverse this rejection.

As discussed above, the claims have been amended to recite the phrase "increased activity of a promoter having a p53 binding site".

This support for this amendment is found on page 7, line 7, of the specification, where the phrase "ING2 activates p53 binding site controlled promoters" is set forth.

In view of the MPEP's guidance that support for a claim amendment need not be *in haec verba*, the Applicants submit that this amendment is fully supported.

Withdrawal of this rejection is respectfully requested.

Rejection of claims under 35 U.S.C. § 112, first paragraph (section 11 of Office Action)

Claims 27, 30 and 32 under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Applicants respectfully traverse this rejection.

The Applicants respectfully submit that in view the amendments and the above general discussion, this rejection has been adequately addressed and may be withdrawn.

Withdrawal of this rejection is respectfully requested.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RIGL-008CIP.

Respectfully submitted,
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Date: April 25, 2005

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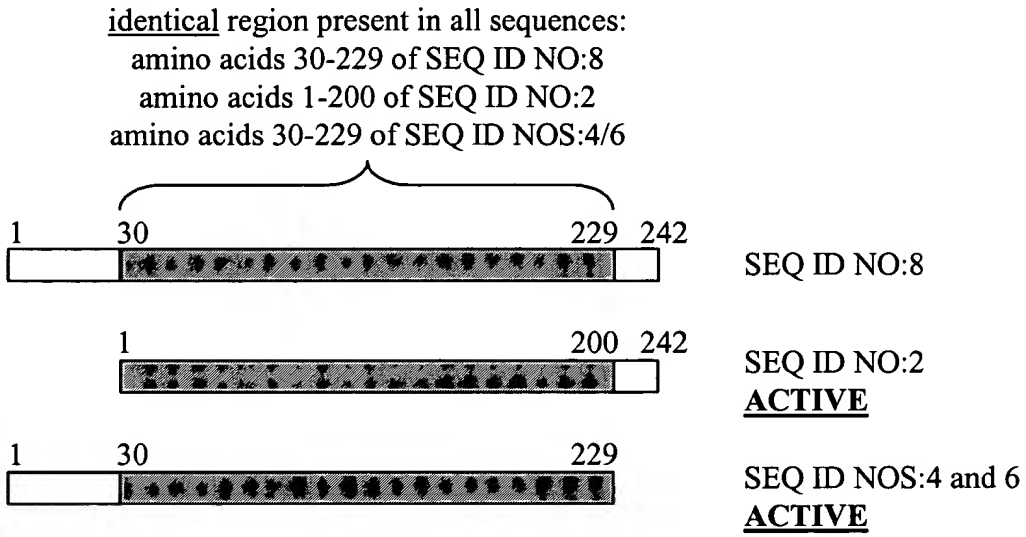
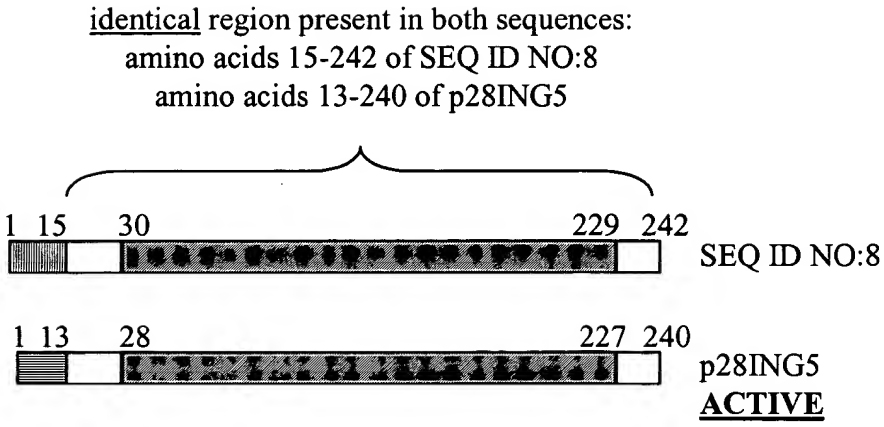
EXHIBIT A

Summary of prior arguments

As illustrated below, SEQ ID NOS:2, 4, 6 and 8 of the instant application, as well as p28ING5 of Shiseki *et al,* are splice variants of the same gene product, and as a result are highly related to each other in sequence.

As indicated by the word "**ACTIVE**", SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and p28ING5 have all been shown to be increase transcription from a promoter having p53 binding sites.





In view of the fact that SEQ ID NO:8 contains a 300 amino acid region that is also contained within each of the active variants, one of skill in the art would reasonable expect that SEQ ID NO:8 would have the same activity as those variants (i.e., an activity that increases transcription from a promoter having p53 binding sites).